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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,244	01/28/2005	Peter Carmelict	DECLE70.003APC	9196
20995	7590	06/04/2007	EXAMINER	
KNOBBE MARTENS OLSON & BEAR LLP 2040 MAIN STREET FOURTEENTH FLOOR IRVINE, CA 92614			CHONG, KIMBERLY	
			ART UNIT	PAPER NUMBER
			1635	
			NOTIFICATION DATE	DELIVERY MODE
			06/04/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)
	10/502,244	CARMELIET ET AL.
	Examiner Kimberly Chong	Art Unit 1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 19 March 2007.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 3-10 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 3-10 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____.
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.	5) <input type="checkbox"/> Notice of Informal Patent Application
	6) <input type="checkbox"/> Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03/19/2007 has been entered.

Status of Application/Amendment/Claims

Applicant's response filed 03/19/2007 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 10/18/2006 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 03/19/2007, claims 3-10 are pending in the application.

Response to applicant's arguments filed 03/19/2007 is moot in view of the claim amendments and new grounds of rejection below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sirois, G. (US2003/0186920) in view of Peichev et al. (cited on PTO form 1449 filed 7/22/2004), Majka et al. (cited on PTO form 892 filed 12/19/2005) and Schmeisser et al. (Cardiovascular Research 2001, 49: 671-680).

The instant claims are drawn to a method of screening for molecules for the treatment of pathological angiogenesis comprising identifying molecules that inhibit the expression and/or activity of prominin-1 and monitoring comprising exposing prominin-1 or nucleic acids encoding prominin-1 to at least one molecule whose ability to reduce the number of blood vessels during the progression of the disease is sought to be determined, wherein determination is by binding of the prominin-1 to the molecule and wherein the binding is by immunoassay.

Sirois teach a method of testing the ability of an antisense compound to bind to a vesicular endothelial growth factor (VEGF) gene and inhibit expression of said gene in vivo (see paragraph 0088 and 0102). Sirois teach angiogenesis is a response to several factors, including VEGF, wherein new capillary vessels are formed and inhibiting VEGF prevents angiogenesis (see paragraphs 0003-0005). Sirois teach pathological angiogenesis is present in many disease states, such as tumor growth and tumor metastasis and compounds inhibiting pathological angiogenesis can be used as

potential therapeutics in certain diseases (see paragraph 0005). Sirois teach an antisense compound which has the ability to bind to and regulate expression of a VEGF can be monitored by an immunoassay wherein the protein is immobilized i.e. Western blot (see paragraphs 0091-0101) or by measuring the formation of new blood vessels (see paragraph 0104). Sirois does not teach screening for a compound that inhibits prominin-1.

Peichev et al. teach tumor growth requires recruitment of active circulating endothelial cells with the ability to migrate and differentiate at the site to mature endothelial cells which would aid in new blood vessel growth. Peichev et al. teach CD34+ cells, a distinct population of circulating cells, co-express AC133 (prominin-1) and VEGF and these distinct CD34+ cells have the capacity to migrate and differentiate into mature endothelial cells and play a major role in angiogenesis (see page 957, last paragraph).

Similarly, Majka et al. teach a method of determining the biological effect of AC133 (also called prominin) comprising administering an antisense oligonucleotide molecule to CD34+ cells expressing AC133 and determining the hybridization of the antisense oligonucleotide to the nucleic acid expression AC133 (see page 58 and Figure 4). Majka et al. further teach monitoring of the CD34+ cells, expressing AC133, ability to form haemotopoietic colonies after treatment with an antisense oligonucleotide targeted to AC133 (see page 58 and Figure 5).

Likewise, Schmeisser et al. teach CD34+ cells co-expressing both AC133 and VEGF receptors have the ability to differentiate into mature endothelial cells.

Schmeisser et al. teach this finding allows for the potential of therapeutic management in patients with pathological angiogenesis (see page 680, last paragraph).

It would have been obvious to one of skill in the art at the time the invention was made to screen for a molecule that inhibits AC133 using the assay taught by Sirois.

One of skill in the art would have been motivated to use the assay taught by Sirois to screen for compounds that inhibit the expression of AC133, given that Sirois teach VEGF's role in angiogenesis and inhibiting angiogenesis is therapeutically beneficial in certain disease states in pathological angiogenesis such as tumor growth. Moreover, because both Peichev et al., Majka et al. and Schmeisser et al. teach certain disease states such as tumor growth is due in part to a certain type of circulating endothelial cells and these cells co-express VEGF and AC133, one of skill in the art would be motivated to screen for a compound that inhibits AC133.

Finally, one of skill in the art would have had a reasonable expectation of success screening for a compound that binds to and inhibits expression from a prominin-1 gene given that Sirois et al. teach screening for an antisense compound that inhibit the expression of a VEGF protein expressed similarly to an AC133 in an endothelial cell and teach measuring the ability of the compound to reduce the number of blood vessels. Moreover, one of skill in the art would have had a reasonable expectation of success given that Majka et al. actually teach an antisense compound targeted to a gene encoding AC133.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 3-10 rejected under 35 U.S.C. 103(a) as being unpatentable over Sirois, G. (US2003/0186920), Peichev et al. (cited on PTO form 1449 filed 7/22/2004), Majka et al. (cited on PTO form 892 filed 12/19/2005) and Schmeisser et al. (Cardiovascular Research 2001, 49: 671-680) as applied to claims 3-6 above, and further in view of Babinet et al. (An. Acad. Bras. Cienc. 2001) and Murphy et al. (US 2003/0045489).

The instant claims are drawn to a method of screening for molecules for the treatment of pathological angiogenesis comprising identifying molecules that inhibit the expression and/or activity of prominin-1 and monitoring comprising exposing prominin-1 or nucleic acids encoding prominin-1 to at least one molecule whose ability to reduce the number of blood vessels during the progression of the disease is sought to be determined, wherein determination is by binding of the prominin-1 to the molecule and wherein the binding is by immunoassay. The claims are further drawn to a method of screening for the treatment of pathological angiogenesis wherein the molecules are identified by providing a mammalian knockout model that does not express prominin-1 and administering said molecule to be tested and wherein the mammal is a mouse and further wherein the model simulates a disease or condition comprising pathological blood vessel formation.

Sirois, Peichev et al., Majka et al. and Schmeisser et al. are relied upon as above. Sirois, Peichev et al., Majka et al and Schmeisser et al. do not teach identification of a molecule that inhibits expression and/or activity of prominin-1 using a knock-out mouse model.

Babinet et al. teach generation of a knockout mouse model for the study of mammalian biology (see abstract). Murphy et al. teach a mammalian knockout model wherein the mammal is a mouse and teach screening of molecules for the ability to inhibit angiogenesis using the knockout murine model (see paragraph 0166).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a mammalian murine knockout model to screen for molecules for the treatment of pathological angiogenesis.

One would have been motivated to make a knock-out mouse model to identify molecules that modulate AC133 because Babinet et al. teach the use of murine knock-out mice is a common way to study the function of genes and more importantly, a way to study the development of appropriate therapies for specific diseases (see page 366). One would have been motivated to make a knock-out model to screen for molecules that modulate AC133 because Murphy et al. teach knock-out animals that simulate a disease associated with angiogenesis are useful to screen for molecules that have anti-angiogenic properties (see paragraph 0167). Further, one would have been motivated to measure the formation of growth of blood vessels during the progression of the disease in the knock-out model of angiogenesis given that Sirois teach measurement of

blood vessel formation is an efficient way to test the antisense compounds inhibitory effects VEGF responsible for angiogenesis in vivo.

Finally, one would have a reasonable expectation of success because Babinet et al. teach generation of a mammalian knockout model, the steps of which are routine to one of skill in the art. Further, one would have a reasonable expectation of success because Murphy et al. teach use of a mammalian knockout model to simulate a disease associated with angiogenesis and the use of the model to screen for compounds that modulate angiogenesis.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Applicant's Arguments

Re: Claim Rejections - 35 USC § 102

The rejection of claims 3-6 under 35 U.S.C. 102(b) as being anticipated by Majka et al. (cited on PTO form 892 filed 12/19/2005) and evidenced by Peichev et al. (cited on PTO form 1449 filed 7/22/2004) is obviated in response to claim amendments filed 03/19/2007.

Re: Claim Rejections - 35 USC § 103

The rejection of record of claims 3-10 under 35 U.S.C. 103(a) as being unpatentable over Peichev et al. (cited on PTO form 1449 filed 7/22/2004) and Majka et al. (cited on PTO form 892 filed 12/19/2005) in view of Babinet et al. (An. Acad. Bras.

Cienc. 2001) and in further view of Murphy et al. (US 2003/0045489) is obviated in response to claim amendments filed 03/19/2007.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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KC
Examiner
Art Unit 1635

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